REMARKS/ARGUMENTS

Claim 7 has been revised to more explicitly state an inherent feature of the claim. No narrowing of claim scope is intended or believed to have occurred.

Claim 8 has been revised to include the features of "non-infectious" and "virus particles" and "tumor specific antigens" as found in pending Claim 1.

Claims 8 and 19 have been revised to include the feature of a "virus-like" particle. Support for this claim is provided at least by original Claim 6, which was canceled with the Response filed March 10, 2009.

Claim 19 has also been revised to be more similar to pending Claim 1.

No new matter has been introduced, and entry of the above revised claims is respectfully requested.

Virus-like particle

Claims 8 and 19 have been revised to feature "virus-like" particle, which was previously objected to by the Office in the Actions mailed August 29, 2008 and February 23, 2009 as well as during the interview on March 5, 2009.

But the Office has now relied upon Wagner et al., and cited documents by Roy, Shimbeck et al., and Greenstone et al., all of which provide clear evidence of the skilled person's knowledge regarding the concept of "virus-like particles" (see, for example, the titles of each document). Thus there is no reasonable basis to allege "virus-like particles" as overlapping with the cells of Hiserodt et al. or Nawrocki et al. Accordingly, Applicant now re-instates the scope of the claimed subject matter to include such particles in Claims 8, 19, 20, 22, 25 and 26.

If the Office chooses to re-assert the position that "virus-like particles" overlaps with the cells of Hiserodt et al. or Nawrocki et al., Applicant respectfully requests a clear demonstration of evidence for this position in the next Office Communication. Applicant respectfully points out that the combination of Hiserodt et al. or Nawrocki et al. with Wagner et

al. indicates that neither Hiserodt et al. nor Nawrocki et al. teach or suggest a "virus-like particle".

Withdrawn rejections

Applicant acknowledges the Office's withdrawal of the previous rejection based upon Hiserodt et al. based on Applicant's arguments that Hiserodt et al. cell lines **do not** produce a virus particle with the same features as the particles featured in the pending claims AND **do not** teach or suggest a method including the administration of any virus particle to induce an immune response.

Applicant also acknowledges the Office's withdrawal of the previous rejection based upon Nawrocki et al. based on Applicant's arguments that Nawrocki et al. cell lines **do not** produce a virus particle with the same features as the particles featured in the pending claims AND **do not** teach or suggest a method including the administration of any virus particle to induce an immune response.

First alleged rejection under 35 U.S.C. § 103

Claims 1-5, 7, 8, 16-20, and 23-26 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hiserodt et al. (USP 6,277,368) and Wagner et al. (Intervirology, 39(1):93-103, 1996). Applicant has carefully reviewed the statement of the instant rejection as well as the cited documents and respectfully traverses because no *prima facie* case of obviousness is present.

As noted above, Hiserodt et al. do not disclose a cell line that produces a virus particle according to the pending claims. Additionally, and as acknowledged in the statement of the rejection (on page 3 of the Action mailed July 17, 2009), Hiserodt et al. fail to teach administering a non-infectious, biologically generated virus particle.

The instant rejection is based on the allegation that it would have been obvious to modify the method of Hiserodt et al. by using the virus-like particle (VLP) of Wagner et al., where the VLP are produced in the Hiserodt et al. cells. Applicants point out that the statement

of the rejection is consistent with the fact that Hiserodt et al. do not teach or suggest producing VLP in their cells (because otherwise, there would be no need for Wagner et al.).

Moreover, and as an initial matter, Applicant points out that Claims 1-5, 7, 16-18, 21, 23 and 24 all feature "virus particle" rather than "virus-like particle". These claims feature a "non-infectious ... virus particle" which is distinct from a "virus-like particle" because a virus particle can be infectious (and inactivated to become non-infectious as featured in Claim 7) while a virus-like particle is never infectious. The instant rejection provides no evidence or explanation of why the VLP of Wagner et al. is sufficient to meet the "virus particle" feature in these claims. There is no teaching or suggestion of "inactivating" a VLP in either Hiserodt et al. or Wagner et al., whether each is taken alone or in combination. So no *prima facie* case of obviousness is possible against Claim 7, or any of Claims 1-5, 16-18, 21, 23 and 24.

With respect to this rejection more broadly, a *prima facie* case of obviousness requires a clear articulation of the reason(s) ***why*** the claimed subject matter would have been obvious (see MPEP 2143 and the case decisions cited therein). But the statement of the instant rejection fails to meet this requirement.

Beginning on page 4, line 5, of the Action mailed July 17, 2009, the statement of the rejection alleges the presence of "motivation" to combine Hiserodt et al. and Wagner et al. by stating the teachings of each and by asserting that

> one of ordinary skill in the art would have been motivated to modify the method of Hiserodt et al using the VLP for inducing a CTL response in cancer patients, since the VLP are non-infectious, non-replicating and provide a safe antigen delivery system for inducing a CTL response in the complete absence of adjuvant according to Wagner et al.

But the above quote is conclusory and does not adequately provide a reason as to ***why*** the skilled person would have made the combination.

For example, there is no evidence of record to show that the Hiserodt et al. tumor cells and tumor cell lines were recognized as an equivalent of the virus-like particles (VLPs) of Wagner et al. Nor is there evidence that the Wagner et al. VLPs were recognized as an equivalent of the Hiserodt et al. cells.

Additionally, Hiserodt et al. fail to teach or suggest the production of any virus or virus-like particle (VLP) with their tumor cells and tumor cell lines. On the other hand, Wagner et al. report the production of HIV-1 VLPs by use of self-assembling $Pr55^{gag}$ proteins that are expressed in insect cells by recombinant baculoviruses (see page 95, left column, first and last full paragraphs). There is no evidence of record, however, of successful expression of an HIV-1 VLP in a tumor cell or tumor cell line like that of Hiserodt et al.

Furthermore, Wagner et al. report their VLPs as containing a V3 peptide of the HIV-1 gp120 protein and that the VLPs stimulated a cytotoxic T-cell response against V3. Thus the report is of an HIV-1 VLP stimulating an anti-viral response. This is in contrast to Hiserodt et al., who report the use of tumor cells and a cytokine producing cell (see column 7, lines 1-9) to produce an anti-tumor response. To combine these technologies, there must be evidence of ***why*** the skilled person would modify the Hiserodt et al. *combination* of tumor cells and cytokine producing cell by attempting to express a Wagner et al. VLP in the tumor cells alone and then using the VLP. Instead of evidence, the instant rejection appears to be based upon the mistaken impression that because each of Hiserodt et al. and Wagner et al. report the production of immune responses, the teachings can be combined. This is clearly inadequate because Hiserodt et al. and Wagner et al. report different methodologies (combination of cells in Hiserodt et al. vs. VLP only in Wagner et al.) to produce different results (anti-tumor response in Hiserodt et al. vs. anti-viral response in Wagner et al.). Given these differences, evidence for the reason ***why*** a skilled person would combine these technologies must be clearly articulated in order to produce a *prima facie* case.

Without clear articulation of a reason ***why*** the skilled person would make the combination, the instant rejection is based upon impermissible hindsight reconstruction using the instant application as the guide for gathering the cited documents and alleging their combination. This is clearly not the standard for obviousness, and so no *prima facie* case of obviousness is possible. So the instant rejection may be properly withdrawn for this reason alone.

In addition to the foregoing, it is well settled law that obviousness must be supported by a reasonable expectation of success (see MPEP 2143.02 and the case decisions cited therein).

But in the instant case, the disclosures of the cited documents fail to provide the necessary expectation of success. As discussed above there is no evidence of record for the successful expression of a Wagner et al. HIV-1 VLP in a Hiserodt et al. tumor cell or tumor cell line.

Assuming for the sake of argument that a VLP can be produced by expressing the Wagner et al. self-assembling $Pr55^{gag}$ proteins in a Hiserodt et al. cell, there is still no evidence of record that a resultant VLP would have the features of the particles in the pending claims. There is no evidence that the alleged VLP would have a cellular membrane comprising "an MHC molecule that presents one or more tumor specific antigens" **and** "a co-stimulatory molecule" from a Hiserodt et al. tumor cell. There is also no evidence that the alleged VLP can "induce an effector cell mediated immune response against tumor cells" as featured in the claims.

Without the required reasonable expectation of success, no *prima facie* case of obviousness is possible, and so the instant rejection may be properly withdrawn for this reason alone.

Applicant points out that as disclosed in the instant application and encompassed by the claims, the intended subject matter requires a virus or virus-like particle to have a cell membrane with both the "an MHC molecule that presents one or more tumor specific antigens" **and** "a co-stimulatory molecule" to "induce an effector cell mediated immune response against tumor cells." This reflects an advance over Hiserodt et al. because 1) a virus or virus-like particle is able to act in place of the Hiserodt et al. tumor cell; and 2) the particle can be used effectively without the Hiserodt et al. cytokine producing cell. Neither of these advances are taught or suggested by Hiserodt et al. or Wagner et al. Accordingly, each advance is an unexpected result relative to the cited documents. Moreover, these unexpected results are

commensurate with the scope of the claims. It is well settled that the presence of unexpected results is indicative of non-obviousness.

In light of the above, there are multiple reasons for the proper withdrawal of the instant rejection. Early withdrawal in this manner is respectfully requested.

Second alleged rejection under 35 U.S.C. § 103

Claims 1, 19, 21 and 22 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Nawrocki et al. (Cancer Treatment Reviews, 25:29-46, 1999) and Wagner et al. (Intervirology, 39(1):93-103, 1996). Applicant has carefully reviewed the statement of the instant rejection as well as the cited documents and respectfully traverses because no *prima facie* case of obviousness is present.

As noted above, Nawrocki et al. do not disclose a cell line that produces a virus particle according to the pending claims. Additionally, and as acknowledged in the statement of the rejection (on page 5 of the Action mailed July 17, 2009), Nawrocki et al. fail to teach administering a non-infectious, biologically generated virus particle.

The instant rejection is based on the allegation that it would have been obvious to modify the method of Nawrocki et al. by using the virus-like particle (VLP) of Wagner et al., where the VLP are produced in the modified cells of Nawrocki et al. Applicants point out that the statement of the rejection is consistent with the fact that Nawrocki et al. do not teach or suggest producing VLP in their cells (because otherwise, there would be no need for Wagner et al.).

Moreover, and as an initial matter, Applicant points out that Claims 1 and 21 feature "virus particle" rather than "virus-like particle". These claims feature a "non-infectious ... virus particle" which is distinct from a "virus-like particle" because a virus particle can be infectious (and inactivated to become non-infectious as featured in Claim 7) while a virus-like particle is never infectious. The instant rejection provides no evidence or explanation of why the VLP of Wagner et al. is sufficient to meet the "virus particle" feature in these claims. There is

no teaching or suggestion of "inactivating" a VLP in either Hiserodt et al. or Wagner et al., whether each is taken alone or in combination. So no *prima facie* case of obviousness is possible against Claims 1 and 21.

With respect to this rejection more broadly, a *prima facie* case of obviousness requires a clear articulation of the reason(s) ***why*** the claimed subject matter would have been obvious (see MPEP 2143 and the case decisions cited therein). But the statement of the instant rejection fails to meet this requirement.

Beginning on page 6, line 1, of the Action mailed July 17, 2009, the statement of the rejection alleges the presence of "motivation" to combine Nawrocki et al. and Wagner et al. by stating the teachings of each and by asserting that

> . one of ordinary skill in the art would have been motivated to modify the method of Nawrocki et al using the VLP for inducing a CTL response in cancer patients, since the VLP are non-infectious, non-replicating and provide a safe antigen delivery system for inducing a CTL response in the complete absence of adjuvant according to Wagner et al.

But the above quote is conclusory and does not adequately provide a reason as to ***why*** the skilled person would have made the combination.

For example, there is no evidence of record to show that the modified cells of Nawrocki et al. were recognized as an equivalent of the virus-like particles (VLPs) of Wagner et al. Nor is there evidence that the Wagner et al. VLPs were recognized as an equivalent of the Nawrocki et al. cells.

Additionally, Nawrocki et al. fail to teach or suggest the production of any virus or virus-like particle (VLP) with their modified cells. On the other hand, Wagner et al. report the production of HIV-1 VLPs by use of self-assembling $Pr55^{gag}$ proteins that are expressed in insect cells by recombinant baculoviruses (see page 95, left column, first and last full paragraphs). There is no evidence of record, however, of successful expression of an HIV-1 VLP in a modified cell like that of Nawrocki et al.

Furthermore, Wagner et al. report their VLPs as containing a V3 peptide of the HIV-1 gp120 protein and that the VLPs stimulated a cytotoxic T-cell response against V3. Thus the report is of an HIV-1 VLP stimulating an anti-viral response. This is in contrast to Nawrocki et al., who report the use of tumor cells (see page 40, Table 2, for example) to produce an anti-tumor response. To combine these technologies, there must be evidence of ***why*** the skilled person would alter the modified cell of Nawrocki et al. by attempting to express a Wagner et al. VLP in the cell and then using the VLP. Instead of evidence, the instant rejection appears to be based upon the mistaken impression that because each of Nawrocki et al. and Wagner et al. report the production of immune responses, the teachings can be combined. This is clearly inadequate because Nawrocki et al. and Wagner et al. report different methodologies (modified cells in Nawrocki et al. vs. VLP only in Wagner et al.) to produce different results (anti-tumor response in Nawrocki et al. vs. anti-viral response in Wagner et al.). Given these differences, evidence for the reason ***why*** a skilled person would combine these technologies must be clearly articulated in order to produce a *prima facie* case.

Without clear articulation of a reason ***why*** the skilled person would make the combination, the instant rejection is based upon impermissible hindsight reconstruction using the instant application as the guide for gathering the cited documents and alleging their combination. This is clearly not the standard for obviousness and so no *prima facie* case of obviousness is possible. So the instant rejection may be properly withdrawn for this reason alone.

In addition to the foregoing, it is well settled law that obviousness must be supported by a reasonable expectation of success (see MPEP 2143.02 and the case decisions cited therein).

But in the instant case, the disclosures of the cited documents fail to provide the necessary expectation of success. As discussed above there is no evidence of record for the successful expression of a Wagner et al. HIV-1 VLP in a modified cell of Nawrocki et al.

Assuming for the sake of argument that a VLP can be produced by expressing the Wagner et al. self-assembling $Pr55^{gag}$ proteins in a Nawrocki et al. cell, there is still no evidence of record that a resultant VLP would have the features of the particles in the pending claims.

There is no evidence that the alleged VLP would have a cellular membrane comprising "an MHC molecule that presents one or more tumor specific antigens" **and** "a co-stimulatory molecule" from a Nawrocki et al. cell. There is also no evidence that the alleged VLP can "induce an effector cell mediated immune response against tumor cells" as featured in the claims.

Without the required reasonable expectation of success, no *prima facie* case of obviousness is possible, and so the instant rejection may be properly withdrawn for this reason alone.

Applicant points out that as disclosed in the instant application and encompassed by the claims, the intended subject matter requires a virus or virus-like particle to have a cell membrane with both the "an MHC molecule that presents one or more tumor specific antigens" **and** "a co-stimulatory molecule" to "induce an effector cell mediated immune response against tumor cells." This reflects an advance over Nawrocki et al. because a virus or virus-like particle is able to act in place of the Nawrocki et al. cell. This advance is not taught or suggested by Hiserodt et al. or Wagner et al. So the advance is an unexpected result relative to the cited documents. Moreover, these unexpected results are commensurate with the scope of the claims. It is well settled that the presence of unexpected results is indicative of non-obviousness.

In light of the above, there are multiple reasons for the proper withdrawal of the instant rejection. Early withdrawal in this manner is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned.

Respectfully submitted,

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